The reason infection with this unusual organism developed in our patient is not clear. Decreased host defenses and major structural abnormalities characterize all previous cases but were not present in our patient. Results of her radiographic and ultrasonographic studies suggested previous pyelonephritis, so we cannot say her urinary tract was unequivocally normal. But it lacked major structural abnormalities, such as vesicoureteral reflux, that would predispose to infection. We have no reason to suspect a primary bacteremia with secondary seeding of the kidney.

The source of the organism is also of interest. *P multocida* organisms have been identified in the upper respiratory tract of healthy persons and patients in hospital.[10,12] Most patients with *Pasteurella* urinary tract infection have been in proximity to dogs or cats and some investigators speculate contact with these animals as a source.[3,11] The female genitalia may serve as a focus of infection—vaginitis, cervicitis and Bartholin's gland abscess have been reported.[2,3,5] There are no data on the role of intentional or accidental direct contact with oral secretions of animals. While there are a few reports of medical consequences of bestiality,[13,14] we could find no literature relating this unusual practice to urinary tract infections. Bestiality was not suspected in this case. Direct contact with oral secretions may not be necessary to cause infection, as the organism can be dormant for long periods.[2] Our patient's dog frequented both her bedroom and her bathroom. The dog's oral cavity was culture-positive for a heavy growth of *P multocida*, and it may have been the source of the infection.

Treatment is uncomplicated in most cases. A characteristic of *P multocida* is its sensitivity to penicillin.[10] Reported cases have responded to penicillin,[10] gentamicin[11] and trimethoprim-sulfamethoxazole therapy.[2] Why our patient's symptoms recurred after a two-week course of ampicillin is not known, but it may reflect a failure of nonparenteral antimicrobial therapy in upper urinary tract infections or patient noncompliance. Moreover, the role of individual antibiotics in this case is obscured by the patient's receiving multiple antibiotics. Her rapid defervescence after parenteral therapy and her uneventful recovery suggest that treatment of *P multocida* urinary tract infections should be straightforward.

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Disseminated Actinomycosis

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ACTINOMYCES ISRAELII, a normal constituent of oral flora, is an opportunistic organism requiring interruption of the mucosal barrier to be pathogenic.[1] Most commonly, actinomycetic organisms burrow without regard for facial tissue planes, resulting in draining sinuses and masses of abundant granulation surrounded by dense fibrous tissue. The following is a report of a case of disseminated actinomycosis presenting with nonspecific constitutional symptoms and radiographic findings. This case shows the indolent nature and diagnostic challenge of this disease.

Report of a Case

The patient, a 41-year-old man with a history of schizophrenia, presented for evaluation of anemia, weight loss and cough. He was well until 1983 when he sustained a massive upper gastrointestinal hemorrhage requiring a vagotomy and subtotal gastrectomy. He recovered without complications and did well until July 1985 when his hematocrit was noted to be low and unresponsive to iron, folate and vitamin B_{12} therapy. Chest x-ray and barium enema films were normal. In addition, he had a six-month history of weight loss and a nonproductive cough for one week. He smoked heavily but said he did not have tuberculosis or chemical exposures and did not abuse drugs intravenously. Findings of a physical examination were significant for cachexia, extremely poor dentition, pulmonary bibasilar rales and right upper quadrant abdominal tenderness. A stool specimen was heme-negative. Laboratory studies elicited the following values: hemoglobin 8 grams per dl, hematocrit 24.6%, leukocyte count 12,600 per μl (65% polymorphonuclear neutrophils, 22% bands), platelets 754,000 per μl, erythrocyte sedimentation rate 143 mm per hour, prothrombin time 14.6 seconds (11.9, control), total protein 9.1 mg per dl, albumin 1.7 mg per dl, alkaline phosphatase 159 units per liter (Westergren), serum aspartate aminotransferase (glutamic-oxaloacetic transaminase) 28 units per liter and serum alanine aminotransferase (glutamic-pyruvic transaminase) 20 units per liter. A chest x-ray film showed many nodular lesions 0.5 to 2.5 cm in diameter predominantly in the lower lung fields (Figure 1). A blood smear showed 1+ macrocytes and microcytes with 2+ rouleaux.

Bronchoscopy and a transbronchial biopsy specimen showed nonspecific inflammation without granulomas. A smear was negative for acid-fast bacilli, and the patient was anergic to skin tests. The patient's condition continued to deteriorate, with daily fevers to 39.4°C (103°F), and his hematocrit dropped to 21%. A bone marrow aspirate and biopsy specimen, taken on day 3 of admission, showed a decreased erythroid series and a normal plasmacyte popula-

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tion at 5% to 10%. Serum protein electrophoresis showed a broad band polygammopathy. A serum iron concentration and total iron binding capacity were 12 and 150 μg per dl, respectively, consistent with anemia of chronic disease. Cultures of blood, bronchial biopsy and bone marrow specimens remained negative.

An abdominal ultrasonogram showed many echodense areas of the liver, and a subsequent abdominal computed tomographic (CT) scan revealed many hypodense masses in the liver (Figure 2). On day 12 a percutaneous fine-needle aspirate of the liver initially showed a predominance of inflammatory cells—mostly histiocytes and lymphocytes consistent with chronic inflammation without evidence of malignancy. The patient was evaluated for an open-lung biopsy; on reexamination of the liver biopsy specimen, however, yellowish granules were noted and subsequent stains showed numerous colonies of gram-positive non-acid-fast filamentous branching rods consistent with *Actinomyces israelii* (Figure 3). Anaerobic cultures grew several species of *Bacteroides* and *Fusobacterium,* but no *Actinomyces*. The patient received penicillin, 2 million units given intravenously every four hours, and became afebrile within 48 hours.

A barium enema study showed a cone-shaped pouch at the hepatic flexure extending superiorly and ending blindly without extravasation of barium (Figure 4). No other irregularities were noted and an upper gastrointestinal series was unremarkable.

The patient received a four-week course of penicillin given intravenously, followed by a five-month outpatient course of penicillin by mouth. He remained afebrile, was without pulmonary symptoms and began to gain weight. On discharge his hematocrit was 27% and his chest x-ray film had cleared.

Discussion

Although *Actinomyces*—from Greek for "ray" and "fungus"—was named in 1878 to describe the filaments radiating from a central tangled mass, it was later (1960) identified as an obligate anaerobic or microaerophilic bacterium.[2] It is a fastidious, weakly gram-positive, non-acid-fast, branching filamentous rod. In an abscess the outer zone of granulation surrounds a center of "sulfur granules," named for their grossly yellow appearance but consisting of entangled masses of the organism contained within a protein-polysaccharide complex that under the microscope is in a ray form, giving a sunburst appearance.[3] The organism is difficult to culture[4,5] and is rarely encountered as a pure isolate. Brown reviewed 181 case records of actinomycosis microscopically confirmed based on lesions with granules of gram-positive branching bacilli seen with a Brown-Brenn

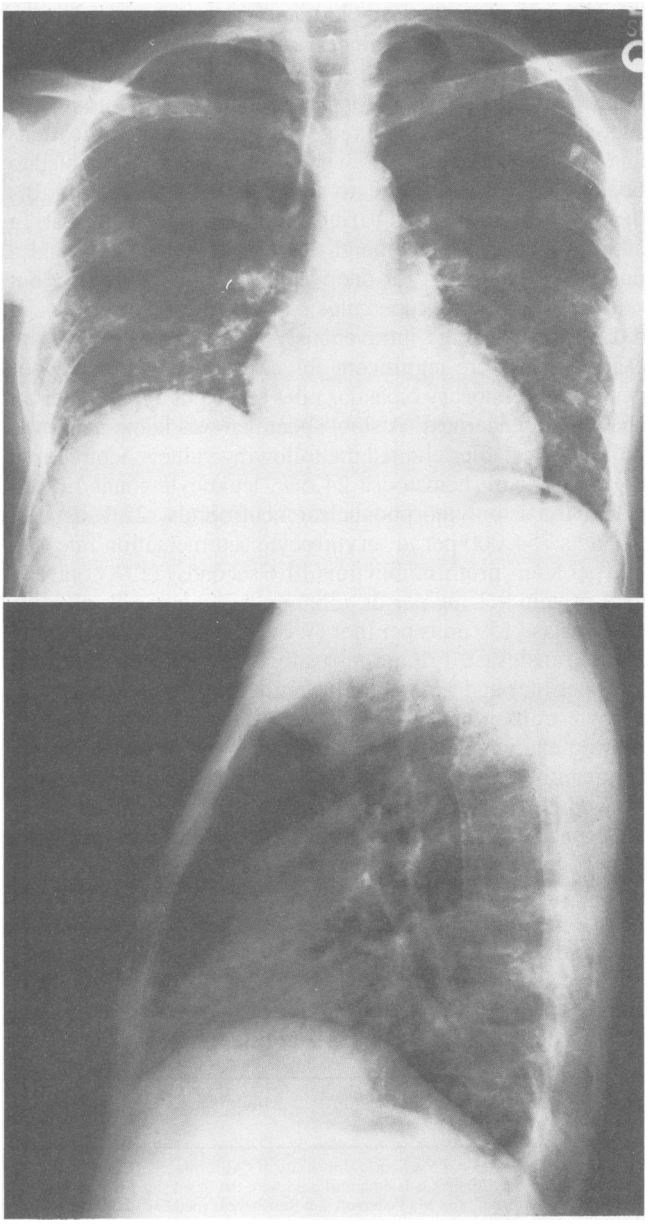

Figure 1.—Chest x-ray films, posteroanterior **(top),** and lateral **(bottom),** show bibasilar multinodular infiltrates.

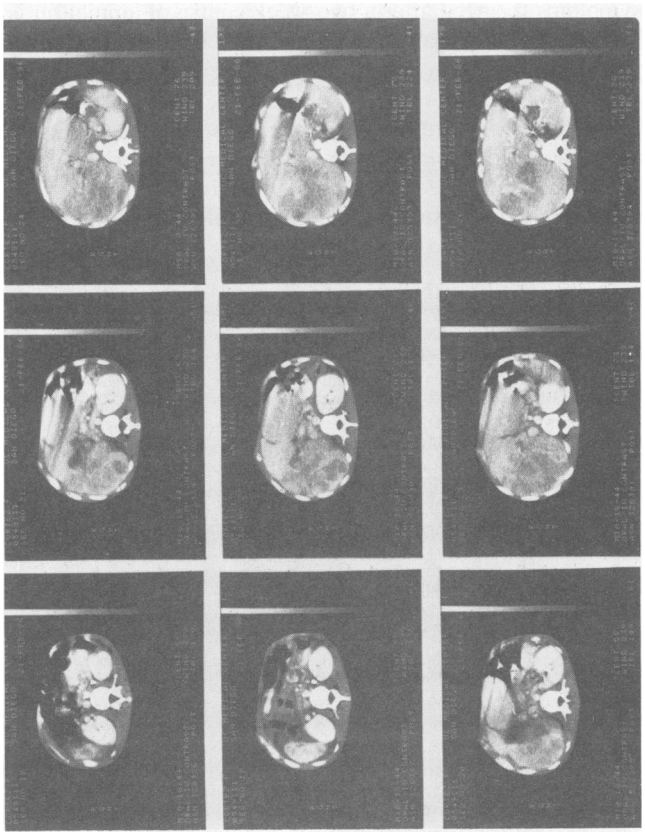

Figure 2.—An abdominal computed tomographic scan shows multiple hypodense masses throughout the right lobe of the liver.

stain. Of the 67 attempted cultures, only 24% were positive for actinomycosis, 46% showed no growth and the rest grew various other bacteria.[6] Holm examined specimens of pus from about 650 patients with closed actinomycotic lesions, and in all instances other microbes were present, particularly coliforms and gram-negative anaerobic bacilli in abdominal sources, and corroding *Bacillus* and *Actinobacillus actinomycetemcomitans* (constituents of oral flora) in pulmonary sources.[7] Successful identification requires careful handling, culturing many specimens in enriched media under anaerobic conditions and carbon dioxide and an adequate time (five to ten days) for growth. Therefore, a definitive diagnosis is usually made on histologic identification of an actinomycotic granule and occasionally by culture. Our diagnosis was made histologically with Grocott's methenamine-silver and Brown-Brenn stains.

Human actinomycosis has five clinical presentations: cervicofacial, thoracic, abdominal, disseminated and pelvic—the last associated with intrauterine contraceptive devices.[8] In Brown's review of 181 patients presenting with the first four types, he found a proportion of about 45%, 25%, 20% and 10%, respectively. The disease can smolder for as long as 15 years before a diagnosis is made; Brown found, however, that 90% were diagnosed one month to two years after the initial symptoms.[6]

Antecedent factors are frequently evident. A dental infection or a manipulation commonly precedes a cervicofacial disease.[4] Aspiration, esophageal penetration or direct extension from the neck and mediastinum can result in a thoracic infection.[3] Disruption of the intestinal mucosa from an appendectomy, gastrectomy, cholecystectomy, diverticulitis, cancer or trauma (blunt or penetrating) can lead to an abdominal infection.[4,5,9,10]

Hematogenous dissemination apparently stems most frequently from an initial pulmonary infection.[11-13] One reason for this association may be the lengthy delay in diagnosis of pulmonary actinomycosis. The clinical picture often mimics tuberculosis or malignancy with nonspecific constitutional symptoms of weight loss, cough, chest pain, fever and hemoptysis going unrecognized until an empyema or chest wall fistula develops.[3] Therefore, this delay in diagnosis and consequently prolonged disease state theoretically provide adequate time for dissemination. The liver is the other organ most commonly involved in disseminated disease, but because isolated hepatic cases are seldom seen, it is more likely that the liver is secondarily infected.[6] Possible mechanisms of hepatic involvement include direct extension from the intestinal wall, portal vein delivery from an infected appendix or colon or hepatic artery transport during general dissemination.[3,14]

Patients present with fever, weight loss, anorexia, nausea,

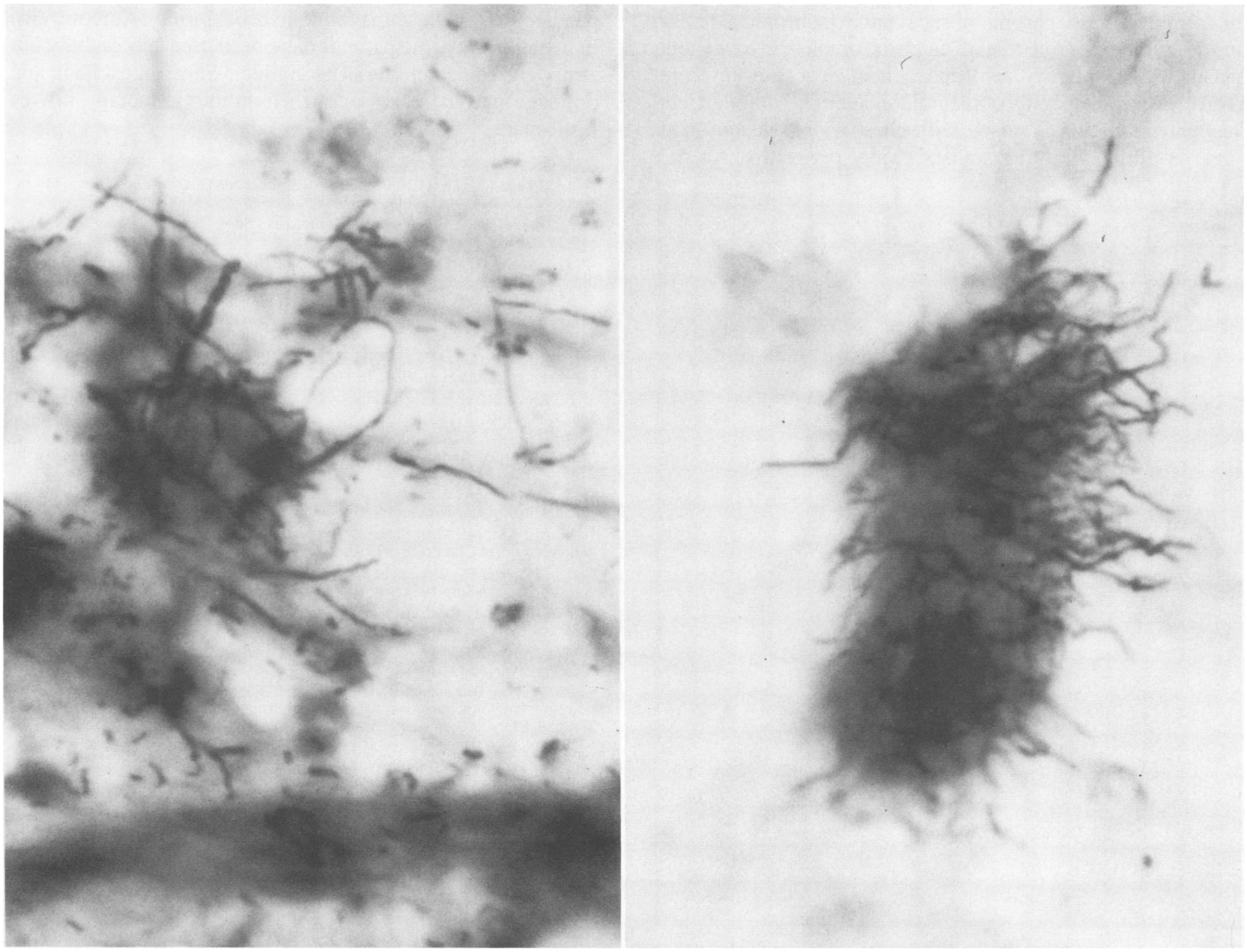

Figure 3.—Microphotographs of a liver biopsy specimen show (**left**) gram-positive, branching filamentous bacilli (Brown-Brenn stain, original magnification × 1,000) and (**right**) a sulfur granule of actinomycosis (Grocott's methenamine-silver stain, original magnification × 1,000).

vomiting and fatigue. A history of temporary resolution of symptoms following a short course of penicillin may be helpful in suspecting *Actinomyces*. Without the presence of a sinus tract or fistula the diagnosis is very difficult. In one series the correct diagnosis was made in only 7% of patients at the time of admission.[4] The differential diagnosis includes miliary tuberculosis, other granulomatous diseases, neoplasm with or without metastases, appendicitis, cholangitis or regional enteritis, especially if sinus tracts are present.

Our patient presents a confusing picture. His poor dentition, which eventually required total dental extraction, is a likely source for pulmonary infection via aspiration of oral secretions. On the other hand, his previous gastrectomy and the cone-shaped colonic pouch resembling a fistula lead one to suspect intestinal trauma as the cause of the hepatic lesions. No evidence of fistulous tracts through the diaphragm could be found to incriminate direct extension between the liver and lung. Therefore, two possibilities exist: a heavily infested oral cavity seeding the lung and the bowel separately or, more likely, hematogenous spread from either a pulmonary or an intestinal primary source, secondarily infecting the liver.

Laboratory findings are also nonspecific: leukocytosis, normohypochromic, normocytic anemia, an elevated erythrocyte sedimentation rate, an increased γ-globulin level,[15] a slightly increased alkaline phosphatase value and thrombocytosis.[16,17] Radiographically, pulmonary involvement can take the form of a mass, chronic fibrocavitary or chronic alveolar infiltrates ranging from a small patch to complete involvement of a lung.[18] Pleural involvement occurs in most cases, evident as an effusion, empyema or pleural thickening. Although less frequent, suspicion is raised with chest wall invasion—soft tissue swelling, draining sinuses, wavy periostitis, rib destruction and with penetration of an interlobar fissure.[18] Actinomycosis of the liver appears as multiple focal defects by technetium Tc 99m sulfur colloid and as intense focal concentration by gallium citrate Ga 67 nuclear medicine scans. This pattern is also seen with malignant neoplasms, lymphomas and pyogenic abscesses.[19] A CT scan in our case showed many hypodense areas in the liver, again a nonspecific finding but an aid in localizing an area for biopsy.

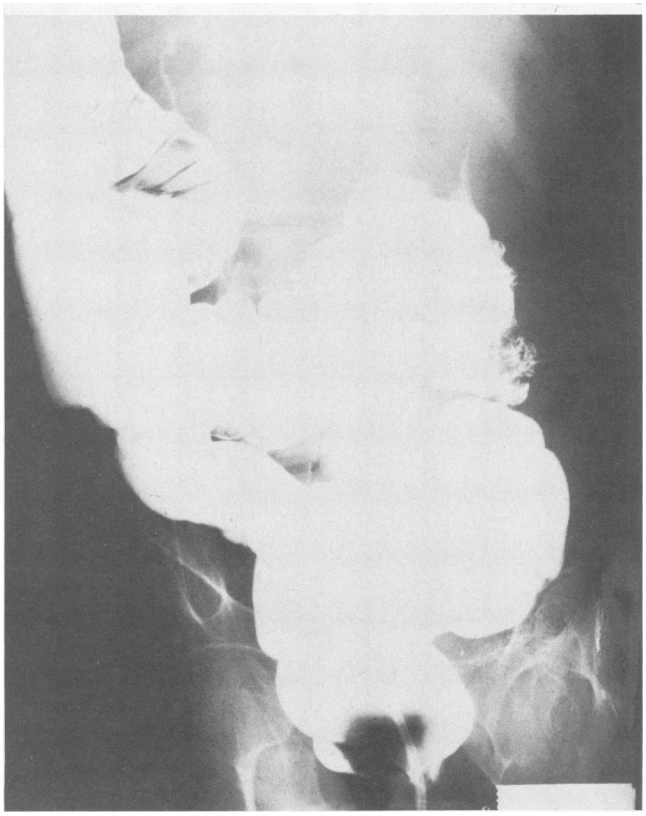

Figure 4.—A barium enema film shows surgical wire in the left upper quadrant and a colonic cone-shaped pouch extending up from the hepatic flexure, resembling a fistulous tract.

Cedermark and co-workers reported a very similar case of a possible neoplasm of the liver with pulmonary metastases.[16] Their patient underwent exploratory laparotomy and hepatectomy of the left lobe to remove a large mass, later histologically proving to be *Actinomyces*. We avoided a surgical procedure in our patient by using CT-guided fine-needle aspiration of one of the hepatic masses. Meticulous examination of the specimen by our pathologist revealed the characteristic sulfur granules and branching rods.

The effectiveness of the use of penicillin in treating actinomycosis is well established.[4] Recommended courses of therapy vary considerably, but it is generally accepted that treatment of disseminated disease must continue for a long period of time. Initial treatment is usually high doses of penicillin given intravenously—10 to 20 million units per day for two to six weeks—followed by penicillin taken orally—2 to 5 million units per day—for three to six months.[3] Tetracycline (the preferred agent), lincomycin, clindamycin, chloramphenicol and chlortetracycline hydrochloride (Aureomycin) in penicillin-allergic patients have been used successfully but aminoglycoside activity is negligible.[2] Surgical excision and drainage may be necessary when antibiotic therapy proves inadequate.[9]

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